

THE PREVALENCE AND CHARACTER OF TUBERCULOSIS IN HONGKONG

BY

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II. THE PORTALS OF ENTRY AND MODE OF SPREAD OF TUBERCULOSIS

The skin route as a portal of entry for tuberculosis which becomes widespread is negligible; the nose and mouth are the only ones worthy of serious consideration, and from the bacillary point of view a certain amount of exchange between the respiratory and alimentary tracts is possible; inhaled bacilli may be returned by ciliary action of the epithelial cells and swallowed, while the latter may in turn rise to the level of the larynx and be inhaled.

That bacilli when ingested can pass through the intestinal walls and affect the mesenteric glands without leaving any trace of their passage is a well-recognised fact, and they may also traverse or grow in and be transmitted from these glands to the lungs and elsewhere.

Experimental evidence goes to show conclusively that a very much larger dose of bacilli is needed to set up the disease by way of the alimentary tract than by the respiratory. In fact, there is considerable difficulty in infecting animals by feeding. As Cobbett states: 'The intestine is well guarded. It is otherwise with the lungs. While not open to the attack of common bacteria in anything like such numbers as is the intestine, it (*i.e.*, the lung) has not developed equal powers of defence, and tubercle bacilli when they enter the bronchi can effect an entrance (*i.e.*, penetration) and cause tuberculosis in numbers which would be powerless for harm if swallowed.' Thus, Gebhardt, working with diluted sputum, found that eight hundred bacilli sufficed to infect by inhalation, while ten to twenty millions failed when swallowed. Kossell, Weber and Heuse found that 1 milligramme would infect calves by inhalation, while one thousand times this dose given by feeding only caused

minimal lesions. More recently, Weber and Titze showed that it requires at least 10 mgrms. of bacilli to infect a calf by feeding, while 1/100 mgrm. may succeed when given by inhalation. Findel infected dogs by inhalation with doses down to 0.14 mgrms., while feeding with doses up to 63 mgrms. produced no effect whatever. Also sixty-two bacilli would constantly infect guinea-pigs by inhalation, even twenty sufficing in some cases, and in very young animals even five. He gave other guinea-pigs doses up to twenty thousand bacilli by feeding, but failed altogether to infect. Many species of animals, including calves, goats, dogs and guinea-pigs, are vastly more susceptible to infection by way of the air passages than by way of the alimentary canal.

The same investigator, Findel, again showed that five million tubercle bacilli when inhaled by a dog caused extensive tuberculosis of the lungs, while one thousand two hundred and twenty times that dose when given by the stomach produced no effect. As regards guinea-pigs, in some experiments as small a number as twenty bacilli were sufficient to cause pulmonary disease when inhaled, whereas the animals were able to withstand three hundred and eighty-two thousand times that dose when introduced into the alimentary canal.

Passing from these animal experiments to human cases, an interesting and instructive example was brought forward by Cautley in which one hundred and fifty-one children and two hundred and nine adults were unconsciously subjected to feeding experiments by consuming milk from tuberculous cows. Of these three hundred and sixty individuals 'only two of the children were affected, and they merely had a mild adenitis. . . They had taken the milk for a year and a year and a half respectively, and the milk was from cows with virulent disease of the udder. Such cases imply that to secure human infection by tuberculous milk the requirements are: youthful age, a badly infected milk, and the prolonged ingestion of such milk.'

Judging from this and the foregoing experimental work, we may say that the probabilities, when one finds what is apparently a primary lung infection, are that the condition has actually arisen by inhalation and not by way of the digestive tract. A more detailed consideration of the site of origin and the mode of spread in individual cases is given later with illustrations from this series.

The tonsils have been regarded by some as the portal of entry

for the bacilli, and they quote tuberculosis of these glands in support of their view. But as there is usually a focus in the lungs as well, it is rarely possible to say whether the primary site of infection was tonsil or lung, or whether both may not be secondary to another portal. As Austin says: 'Examples of apparently isolated tuberculosis of the tonsils should be regarded with reserve, as the presence of latent foci in the lungs can never be excluded.' Excised tonsils of forty-five children (aged $2\frac{1}{2}$ to 15 years) examined for tuberculosis by inoculation into guinea-pigs, by histological examination of sections, by cultures and by smears, all proved negative except one inoculation; we can say, therefore, that infection of the tonsils is uncommon alone. In fact, in most cases of tuberculosis of the tonsils lesions are found elsewhere, especially in the cervical glands, and it is rare to find tubercle bacilli in tonsils of children without clinical evidence of tuberculosis.

'By those who hold that pulmonary infection arises through the cervical glands,' says Dr. Whipham, 'various routes by which the tubercle bacilli may gain access to the lung have been suggested: first, that from the cervical glands they enter the lymph stream, and by means of the lymphatic vessels enter the venous system, and so are conveyed to the lungs; secondly, that their path is from the cervical to the supraclavicular glands, and thence to the apex of the lung; thirdly, that from the cervical they pass to the bronchial glands, and thence are conveyed to the blood-stream and the pulmonary tissues, though in this connection it must be remarked that no communicating channels between the cervical and bronchial glands have been shown to exist.'

The usual modes of entry and extension are, of course, the following:—

(1) Mechanically with air, food, secretions, and so on, as for example when inhaled bacilli lodge in some spot and produce a focal lesion or are returned by the action of the ciliary epithelium, as has been mentioned already; or a focus having formed, the material bearing organisms finds its way into a bronchus, the bacilli pass out and are swallowed or are drawn into another bronchus to set up the condition afresh there.

(2) By direct extension through the tissues with caseation of the parts first affected and involvement of the new tissues by contiguity.

(3) By way of the lymphatic channels which become invaded by

this contiguous extension. The bacilli thus pass to the next lymph-node, and so on by the lymphatic vessels till the thoracic duct conveys them to the left subclavian vein and the lymphatic mode of spread then becomes

(4) Dispersion or distribution by way of the blood-stream; thence they spread by the right side of the heart to the pulmonary arteries, and so to the lungs generally. Or, by the extension of a focus and erosion of the wall of a blood-vessel, they may pass by way of the pulmonary veins to the left side of the heart and thus to the whole systemic arterial distribution. Or yet again, by opening into a smaller artery will invade the area supplied by that vessel.

Cobbett, in his summing up, expresses his opinion in these words: 'While I have no doubt that tuberculosis is frequently of intestinal origin, especially in children, inhalation is the common mode of infection, not only in phthisis, but in other forms of tuberculosis, especially those in which the bronchial glands seem to be the parts first affected.'

In temperate climates isolated primary tuberculosis of the intestines, rarely seen in adults, is not uncommon in children (estimated at 25 per cent. according to some authorities); in tropical countries, judging from my experience in the West Indies (Jamaica) and the Far East (Hongkong), this route, or rather portal of primary entry, is not proportionately so common. Moreover, in temperate climates primary intestinal tuberculosis in children is usually ascribed, if not always traced, to the swallowing of the bacilli in quantities in infected milk. This is certainly not the case here.

It is probable that the intestinal infection is in the majority of cases secondary to lung tuberculosis from swallowing the sputum, even in children, and when definitely primary is due to direct ingestion of the bacilli from dried sputum in infected dwellings.

With this preliminary clearing of the ground we are in a position now to examine the extent to which these conditions as regards the portals of entry are borne out in my series.

Of the whole three hundred cases there were two hundred and nine in which the primary portal of entry appeared to be by the respiratory tract, *i.e.*, 69.66 per cent., and in seven others which are discussed later there was considerable evidence in support of the

same portal, bringing the total to two hundred and sixteen, or 72 per cent.

Only thirty-two have been definitely determined as being of alimentary origin, *i.e.*, 10·66 per cent.; five more, discussed below, were very likely alimentary; this would bring the total to 37, or 12·33 per cent.

In four other cases there was a possibility of almost simultaneous entrance by way of the respiratory and alimentary tracts. In the remaining cases the primary portal was uncertain. A few remarks are given subsequently on each of these.

The number of cases occurring in adults in this series is proportionately small, insufficient at present to form a useful basis for study in detail, and the main objects of this investigation have been the prevalence and character of the disease in children. Of the three hundred cases there were two hundred and twenty-five of ages up to ten years, and each consecutive hundred contained very similar proportions; thus there were seventy-six in the first, seventy-three in the second, and seventy-six in the third. As regards the sex and ages of those comprising the three hundred, the table (see p. 225) shows that one hundred and fifty-five were males and one hundred and forty-five females. It will be noted that after adult life the cases in males preponderate. Whereas in children up to the age of ten years the proportion of males to females is about as 4 : 5, after the age of twenty years the proportion is as 3·6 : 1. This does not mean that the males are more subject to tuberculosis in adult life than are females. When ill the Chinese exhibit strongly the homing instinct, and make every effort to return to their birthplace to die. The females can more easily do this; the males would if they could, but they in many cases have to remain at work until it is too late.

Of the two hundred and twenty-five children under ten years of age there were one hundred and twenty-six females (*i.e.*, 56 per cent.) and ninety-nine males (44 per cent.). This is not of much significance when we bear in mind that the female child in China is not considered of much account, and among the poorer classes from which these records have been made, the females are less well looked after. This is shown by the relative proportions of sexes for the early months of life.

Of the two hundred and twenty-five cases under ten years of age, then, one hundred and forty-eight, or 65·77 per cent., were found in whom the portal of entry was respiratory, and in five others (discussed later) there was a strong probability of a respiratory origin, in which case the percentage increases to 68.

Only thirty-one of these two hundred and twenty-five cases appeared to be definitely of alimentary origin, *i.e.*, 13·77 per cent., while among those of 'uncertain portal' were three others in whom the evidence for the alimentary route had considerable weight; if these be included the total percentage would be 15·11. Cases of isolated primary tuberculosis of the intestine are very rare here in my experience. In fact, only four were met with, namely, Nos. 7, 8, 81, and 112. The great majority, then, have a respiratory portal of entry, the proportion to alimentary being as great as between four and five to one.

In the following the primary portal was not determined with certainty. It will be of interest to give a brief note on each of them.

No. 15. Female, aged 22 months.

The extensive spread of miliary tubercles in the lungs, the meninges, liver, spleen, etc., indicate spread by the systemic blood-stream, possibly after the pulmonary circuit, but the only focus found was the caseating right bronchopulmonary gland; how this became affected without some preceding lung focus I cannot say, but minute search failed to find any. Except for the gland all the tubercles appeared to be of the same age and recent.

No. 27. Female, aged 1 year.

There were two foci in the lower lobe of the right lung and miliary of the same lung with corresponding glandular affection, the gland at the left hilus probably by extension, the left lung not being affected. The intestine showed tuberculous ulceration and the mesenteric glands were in large caseous masses; the spleen was the only viscus with tubercles. If the primary portal were alimentary and the spread to the lungs via the thoracic duct, one would expect both lungs to be involved. In favour of the respiratory origin of the lung condition are the foci in the right lower lobe and the glandular involvement. The ages of the pulmonary and the intestinal conditions would appear to be about the same, and there is the possibility of the simultaneous entry by both routes.

No. 33. Female, aged 4 years.

A few miliary tubercles were scattered throughout the right lung and over the right visceral pleura; the superior tracheo-bronchial gland on the right was enlarged and contained creamy pus; the hilus glands were swollen. The left lung and glands showed no involvement. There were a few miliary tubercles over the spleen surface; miliary also at the base of the brain, especially about the interpeduncular space. Minute search failed to find any focus, unless the glandular abscess constituted it.

No. 34. Male, aged 1 year.

In this case the broncho-pulmonary glands and some of the tracheo-bronchial were enlarged and caseous; minute search, however, failed to find any focus in either lung. The mesenteric glands were also, some of them, enlarged and caseating, but not adherent. The state of the mediastinal glands would warrant one in expecting to find a lung focus. In this connection may be quoted the results of experimental work by Calmette, Guérin, and Breton. They found that in guinea-pigs dying in two to four weeks after being fed on the bacilli the mesenteric glands (especially the superior deriving from the small intestine) were enlarged and inflamed, although no trace of any intestinal lesion could be determined. After 6-7 weeks these glands were caseous in greater or less degree and the lungs showed involvement by miliary tubercles with affection of the corresponding tracheo-bronchial glands. Hence in the present case the probability might seem to be primarily alimentary setting up mesenteric adenitis and mediastinal glandular affection secondary to this.

N. 35. Female, aged 2 years.

Infection extensive: broncho-pneumonic phthisis of the right lung with cavitation in the middle lobe; the left lung contained miliary tubercles all through, but no focus; mediastinal glands, as would be expected, were more affected on the right. The intestines showed numerous ulcers, one having perforated, and the mesenteric glands were large and caseous; the liver and spleen showed miliary tubercles, the latter more than the former, but the kidneys and brain showed none. The intestinal ulceration being so extensive, together with the condition of the mesenteric glands, favour the infection being primarily alimentary whence extension took place via the thoracic duct to the lungs, though the right lung was more affected than the left. On the other hand there had been time for cavitation to arise so that the intestine might have become involved through the swallowing of infected sputum. Here again the respiratory and intestinal conditions did not appear to differ greatly in age, and it is quite possible that the two-fold route was taken. One must always remember that to infer the relative ages of two tuberculous lesions from the stages present is a proceeding liable to fallacy.

No. 39. Male, aged 8 years.

This case showed widespread infection though the course of the extension is difficult to trace. The oldest sites would appear to be: (i) The left mastoid which was caseous and necrosed. As there was middle ear disease this may have been a condition apart from the tuberculosis; although caseous and necrotic, there was no actual proof of its being tuberculous in nature. (ii) Chain of large caseous cervical glands, more on the right than on the left. (iii) Thick caseous adherent peritoneum and mesentery as a vast cheesy sheet. (iv) Chain of large caseating mediastinal glands in relation to both lungs. (v) Focus in upper lobe of left lung. (vi) Mesenteric glands in large caseated masses. Other serous membranes—pleura and meninges—showed merely small miliary tubercles, in the latter limited to the base and not very numerous; the viscera—liver and spleen—showed none on section, merely a few on the surface; the kidneys none, and the intestines none, except miliary on the peritoneal surface. The disease would, therefore, not seem to have been a generalised blood-stream infection.

Was the primary portal of entry the intestine, affecting the mesenteric glands and the peritoneum without leaving any trace in the intestine itself, and thence spreading via the thoracic duct to the lungs? Or was the mastoid primary, thence

affecting the cervical glands (but the mastoid affected was the left while the glands were more marked on the right), and so by the blood-stream the lungs? Or were the cervical glands affected via the tonsils (they showed no signs themselves), and thence the ear and lungs? Or, lastly, was the primary route respiratory, thence to the mediastinal glands and to the blood-stream, and by the sputum to the alimentary canal?

No. 50. Male, aged 3 years.

Focus in the left upper lobe and miliary throughout both lungs; extensive intestinal affection—ulcers in both large and small intestines, mesenteric glands in caseous masses. Miliary tubercles in liver, spleen, and kidneys, but not in the meninges or brain. The alimentary appears a little older than the respiratory. The question is whether there was infection by double route, respiratory from the focus in the upper lobe of the left lung, and the intestine separately, or whether intestines first, thence by the mesenteric glands to the thoracic duct and lungs and then generalised; but, if so, why should the meninges not show any involvement? Or, again, the lung focus may have been the primary condition, the intestines have become affected from that by swallowing the sputum, and from the intestines the mesenteric glands, the lymphatic system, thoracic duct, superior vena cava, and again the lungs to produce the miliary condition there.

N. 52. Female, aged 4 years.

The distribution in this case was fairly general but showed certain peculiarities. There were a few minute tuberculous ulcers in an early stage in the small intestine with tubercles on the corresponding serous surfaces. The mesenteric glands, though not large nor adherent, were caseous. The peritoneum and omentum were thick and studded all over with tubercles varying from miliary to the size of large hempseed. As regards the viscera, the liver and still more the spleen showed miliary and grey tubercles, but on the surface only, none were seen on section. A remarkable thing, however, was that the ovaries were both enlarged, almost to the size of adult ovaries, and contained caseous masses, or rather consisted of a caseous mass in each case, the left a little larger than the right. The right lung contained two foci in the lowest lobe, the size of a pea, miliary tubercles throughout, and a more closely-packed mass of grey tubercles subapical in position; the superior tracheo-bronchial and tracheal glands were enlarged and caseous. The left lung showed miliary tubercles throughout, with closely-packed milia on the somatic pleura; none such were seen on the right. The pericardium also showed several miliary tubercles. There were a few scattered tubercles along and just above the right Sylvian fissure and some at the interpeduncular space. Which was primary is largely a matter of conjecture. For a single organ the ovary was the most extensively involved, each being converted practically into a cheesy, almost creamy, mass. The two lung foci had a fairly hard caseous consistence and were well defined. The alimentary tract tuberculosis and the serous membrane involvement, particularly the latter, were extensive, of the miliary type, though, as stated, a few of the glands were caseous.

No. 54. Female, aged 7 months.

Distribution widespread; from appearances the respiratory and alimentary involvements seemed to be of about the same age. There was a focus at the lower edge of the right upper lobe, extending a little into the middle lobe; miliary and grey tubercles were present elsewhere in the lungs, and the glands were caseous. Alimentary: ulcers in the small intestine, mesenteric glands adherent and caseous,

but not fused ; liver and spleen showed a few miliary tubercles. The right kidney had a small mass occupying the pyramid at the lower pole. The meninges at the base contained several miliary tubercles. A cervical gland on the right side was enlarged and beginning to break down in the interior. The question is whether the lung focus was the primary (the enlarged gland on the same side would support this) from whence extension occurred to the blood-stream to be generalised and by swallowing of the sputum the intestinal condition ; or, whether from the lung primarily to the intestine and mesenteric glands, and by the lymphatic system to the pulmonary circulation to set up the miliary tubercles there ; or, lastly, lungs and alimentary tracts together, then generalisation from the lungs to the systemic vessels and from the alimentary tract by the glands to generalisation in the lungs again.

No. 55. Male, aged 3 years.

The right lung showed tuberculous broncho-pneumonia of the middle and lower lobes ; the upper appeared to be quite unaffected. The middle contained at the lower part a cavity the size of a cobnut. The left lung consisted of three lobes and showed small ulcerated cavities throughout, the average the size of a pea, but rather larger in the middle lobe. Against the lung being primary is the fact that in spite of the extensive tuberculous condition of the organ the glands, though a little swollen and congested, showed no obvious tuberculous infection. On the other hand, the mesenteric glands were enlarged and three of them were caseous, almost chalky, though the intestines showed no change to the naked eye. The possibility is that the alimentary route was primary and thence affecting the lungs by the lymphatic system, the upper lobe escaping, and the hilus and other mediastinal glands not having become tuberculous before death supervened ; or that, since the pulmonary condition was broncho-pneumonic (rather than miliary by way of the pulmonary circulation), the disease had originated by the respiratory route and the alimentary tract had become involved by swallowing the sputum.

No. 58. Male, aged 14 months.

In spite of the age of this child the conditions were such that the general distribution of the disease makes it a matter of conjecture as to the primary portal of entry. There were signs of tuberculous broncho-pneumonia throughout both lungs, with ulceration in the left lower lobe. Generalisation by way of the blood-stream may have taken place from this, causing the deposition of tubercles in liver, spleen, kidneys, and brain. The intestinal ulceration and the masses of caseous mesenteric glands may have arisen from swallowed sputum, but the intestinal condition appeared to be equally advanced as the pulmonary and may have arisen independently. The pericardium also was studded with miliary to pin-head tubercles.

No. 59. Female, aged 4 years.

There was marked kyphosis from extensive involvement of the vertebrae. The spinal site was probably the oldest. From the number of ulcers in the intestines, the large and small both being involved, and the mesenteric glands being in large caseous masses, the alimentary tract would appear to have been attacked prior to the lungs. The latter showed miliary tubercles throughout, but there was also a fair-sized focus (cobnut) just below the apex of the right lower lobe in an early stage of caseation.

No. 65. Female, aged 8 months.

The peculiar limitation of the disease in the lungs to the middle lobe of the right, which contained a distinct focus the size of a pea and small miliary and grey tubercles throughout that lobe, would be in favour of a primary (or at least independent) lung involvement, the alimentary tract being affected secondarily from swallowing the sputum. The mesenteric glands, however, were in large caseating masses and appeared to be of older standing than the pulmonary condition.

No. 66. Female, aged 20 months.

In some respects similar to the last. In this case the lung affection was limited to the right upper lobe in which there was a subapical focus, and in addition generalisation of small tubercles throughout that lobe. The disease was much more advanced in the alimentary tract—intestinal ulceration and large caseous masses of mesenteric glands—and this would point to an alimentary portal of entry. It is not improbable that the lung infection, though later, was independent of the intestinal. The condition of the brain (cerebellar mass) and meninges (miliary to hemipseed on vertex and base) point to dissemination by the blood-stream, but no other viscera showed involvement, to the naked eye at least.

No. 68. Male, aged 3 years.

This case is remarkable in that, except for a hilus gland and a paratracheal gland on the right side as large as a cobnut and filbert respectively and caseous, no focus was found after careful search. There were sparse miliary tubercles throughout both lungs; in the meninges they were numerous, especially at the base, the interpeduncular space, the ependyma, along the Sylvian fissures, and a few on the vertex. The spleen showed also a few milia on the surface. There was no evidence of tuberculous affection of the intestines.

No. 70. Female, aged 7 years.

In this child there was a mass of caseating glands on both sides, involving the inferior and superior tracheo-bronchial and the paratracheal, more on the right than the left; the broncho-pulmonary were not apparently affected. No focus was found in the lungs. The tonsils were not affected, nor the cervical glands, and the spine was examined without success. The alimentary tract was free. In the kidneys, however, there were in the left miliary and grey tubercles, not numerous; in the right more, and arranged almost focally as a group at the base of a pyramid towards the lower pole.

No. 92. Male, aged 10 years.

The primary portal in this case was probably alimentary. There were several ulcers, more in the large than small intestine, however, and a thickened tuberculous mass like a collar at the ileo-caecal valve. Mesenteric glands were enlarged, in masses, and caseating. The lungs showed tubercles varying in size from pin-point to small pea throughout, but the mediastinal glands did not show any tubercles visible to the naked eye, and only one was a little congested and swollen. Neither brain, liver, nor spleen showed any signs, but the kidneys were severely diseased. The right had the pyramidal areas hollowed and caseous; they had run together and were lined by thick tuberculous matter. The left was in a similar condition but to a less degree; calyces opening into each other with a lining of tuberculous pus. The tuberculosis was, therefore, widespread, but if by way of the blood-stream it is peculiar that the kidneys should have been

extensively affected while the brain, liver, and spleen escaped. The lung condition appeared to be more recent than the intestinal and may have arisen by way of the pulmonary circulation as previously pointed out.

No. 95. Female, aged 8 years.

In this case one of the inferior tracheo-bronchial glands was caseous and one of the superior in an earlier stage, both on the right side, but minute search failed to find any tubercles in the lungs. The intestines were not affected, and no focus was detected anywhere. The meninges showed miliary tubercles in fair numbers at the base, fewer along the Sylvian fissures, and only an occasional one at the convexity. No tonsillar or retro-pharyngeal affection was detected. If the meningeal condition arose by inhalation, via the ethmoidal canals (as meningococcus may pass), then we have no explanation of the mediastinal gland affection. Anyway these do not appear to be accounted for, though the spread may have been from them by the blood to the meninges.

No. 96. Female, aged 9 years.

In this case both the respiratory and alimentary tracts showed such extensive involvement that the only doubt is whether the lungs, which were in a state of tuberculous broncho-pneumonia throughout, with cavitation in the right upper lobe and considerable ulceration in the middle lobe, were the primary seat and the intestine was involved later through swallowing the sputum, or whether the alimentary tract formed the primary portal of entry. The small intestine contained tuberculous ulcers; the mesenteric glands were in large caseated masses and adherent, and the peritoneum was studded with tubercles. Of course, there may have been infection by both routes nearly simultaneously.

No. 100. Male, aged 5 years.

In this child there was a cavity in the right upper lobe the size of a medlar, with grey tubercles surrounding it and smaller ones at a greater distance. No other part of the right lung was affected and the left showed nothing. There were pleural adhesions at the apex and direct communication with a tuberculous ulcer the size of a crown-piece above the right clavicle. Whether a supraclavicular gland had become infected from the lung direct and had then opened on the surface, or whether there was a primary affection of the skin which ulcerated and extended to the lung is doubtful. There was a tuberculous skin affection with early ulceration on the right cheek also. No other viscera showed any involvement, and no cervical glands were found enlarged. This may be an example of the mode of spread already mentioned.

No. 104. Male, aged 16 months.

In this the disease was widespread and the primary portal and mode of extension doubtful. The left lung showed two foci, one subapical in the lower lobe, the other nearer the lower edge, and each was surrounded by a zone of small caseating tubercles. The right upper and lower lobes contained miliary tubercles; the glands, hilus, and tracheo-bronchial were caseous and enlarged. In the alimentary tract there was nothing, but one or two mesenteric glands contained small foci. Milia were present in the liver, more and larger in the spleen. The meninges had masses of miliary tubercles at the base, and along the Sylvian fissures and in the interpeduncular space; a few on the vertex and internal surfaces of the cerebral hemispheres. The spine showed a large abscess the size of a Tangerine orange, involving the 11th and 12th dorsal and the 1st lumbar vertebrae. Sug-

gested method of spread : Lung (left), then by inhalation the right, by the blood-stream to the liver, spleen, spine (injury possibly determining this site), and also by the sputum to the intestine and mesenteric glands ; or, from the left lung foci by the sputum to the intestines and mesenteric glands, thence by the lymphatic system to the heart and pulmonary circulation, causing the miliary tuberculosis of the right lung, and also by way of the blood-stream from the lung to the liver, spleen, and meninges. But the spine focus must have been of considerable standing, for there was marked caries and an abscess formed containing caseous matter.

No. 116. Female, aged 10 months.

The right lung showed two distinct foci in the upper lobe : the larger subapical the size of a cherry and caseous, the smaller the size of a pea, near the interlobar fissure ; the rest of the lung contained miliary tubercles. The left lung showed miliary to pin-head tubercles, sparse in the upper lobe, more in the lower. The mediastinal glands were enlarged, with caseating foci. The mesenteric glands (the upper set) were in a similar condition. The question is whether both the respiratory and alimentary tracts were involved simultaneously, or whether the lung focus was primary, the alimentary secondary, passing to the glands without leaving signs in the intestine itself. Thence by the lymphatic to the pulmonary circulation to set up the miliary tuberculosis there, and from the lungs via the blood-stream to the meninges, liver, and spleen. But, if so generalised, one would hardly expect the kidneys to escape altogether.

No. 118. Female, aged 3 years.

In this case the disease was exceedingly widespread and the portal of entry is a matter of conjecture. There were tuberculous ulcers of the right cheek, jaw, and neck ; the right parotid, the submaxillary and cervical glands on both sides, were caseous. There was tuberculous broncho-pneumonia throughout both lungs, the pleura showed many tubercles at the upper part of the somatic layer and all over the visceral ; the pericardium was also affected. The peritoneum was studded with tubercles, miliary to pea, and the intestines contained a few tuberculous ulcers, both in the large and the small ; the mesenteric glands, both upper and lower series, were enlarged, adherent, and caseated. The liver showed a few miliary, the spleen more and somewhat larger. In the right kidney was a small mass of aggregated tubercles at the lower pole, while in a corresponding situation in the left was a definite caseous focus the size of a cherry. There were aggregated miliary tubercles on the basal meninges, a few also on the vertical.

No. 137. Male, aged 10 months.

Disease was widespread and severe in this child, especially when one considers the age. The lungs showed a cavity in the lower lobe, a caseous focus in the middle, and miliary tubercles throughout the remainder of the right ; in the left there were two caseous foci the size of a pea in the upper lobe, a caseous mass as large as a walnut in the lower, and grey tubercles through the rest of the lung. All groups of the mediastinal glands were involved. The mesenteric were enlarged, caseous, and matted, but appeared to be more recent than the thoracic. There were two tuberculous ulcers in an early stage in the small intestine. The femoral glands on each side were the size of a small walnut and caseous (the origin of these could not be discovered). The cervical glands on each side were caseous, especially on the right. The right kidney contained a small aggregation of tubercles at the lower pole ; the liver a few miliary tubercles, the spleen more and larger. The meninges were not affected. As the respiratory and alimentary tracts were both

involved, and also some glands unconnected with either, it is difficult to say which was the primary portal, but the lungs would seem to be most involved and of oldest standing.

No. 141. Male, aged 10 years.

The oldest site in this case was to the right of the sixth cervical vertebra. The bone was carious, and there was a sac with pus discharging from it along the spine into the right pleural cavity (it may possibly have started as a retropharyngeal abscess). The right lung showed miliary tubercles throughout, not very numerous, but more in the upper lobe than in the other two. The left lung had none. There was a caseous gland at the right hilus. Tuberculous sinuses were present in both femora and in the left tibia.

No. 145. Female, aged 2½ years.

Judging from the appearance, degree of caseation, etc., the primary portal may have been alimentary, but the disease was very widespread, the brain showing several foci. There were tuberculous ulcers in both large and small intestines, and the mesenteric glands were in adherent, caseous masses. The cervical gland infection was of fairly long standing also, those on the right containing creamy pus, those on the left being in a caseated stage. Both lungs showed grey tubercles, and the mediastinal glands were in caseous masses at the hilus and along both sides of the trachea. The brain showed: three distinct foci in the left lobe of the cerebellum, another in the right hippocampus, another in the left superior frontal, all these about the size of a pea or a little larger, and in the right supra-marginal gyrus one as large as a cherry—an extensive series of brain foci.

No. 149. Female, aged 3 years.

It is possible that the alimentary portal was the primary as this tract showed the greatest involvement (not a very safe indication, it is true). There were numerous ulcers in both large and small intestines, the mesenteric glands, both upper and lower series, were enlarged, adherent, and caseous. The lungs contained closely aggregated miliary and grey tubercles throughout, but no focus, although the mediastinal glands on both sides were caseous and the paratracheal on the right contained creamy pus. The brain was considerably involved: there were a few miliary tubercles in the basal meninges, many along each Sylvian fissure, and a few on the opposed surfaces of the cerebral hemispheres; in the cerebellum at the fore part of the left hemisphere on the upper surface there was a 'solitary' tubercle, as large as a cherry, and towards the posterior another focus the size of a haricot: on the under surface of the right hemisphere was one the size of a filbert situated anteriorly, and at the posterior extremity another the size of a pea. As regards the course, it does not appear likely that the large tubercles in the cerebellum would be of the same standing as the miliary in the meninges. The intestinal appeared to be the oldest, the lungs probably secondary to this via the pulmonary circulation, for the distribution was equal over both lungs which were granular everywhere from miliary and grey tubercles. General blood infection was supported by the presence of a few tubercles in the liver, spleen, kidney, and meninges, and probably an earlier blood infection set up the various brain tubercles.

No. 157. Male, aged 5 years.

Lungs were granular in appearance from the presence of numerous grey tubercles. A gland at the right hilus was swollen and congested, but showed no signs of tuberculosis in it. Intestines nil. One mesenteric gland, the size of a pea,

contained small grey points. Both kidneys showed miliary tubercles, the left a little more than the right. There were milia also in the liver, spleen, and meninges. No focus could be found. The universality and evenness of the pulmonary distribution point to a haemic infection of the lungs rather than a respiratory.

No. 159. Female, aged 8 years.

The condition in the lungs and in the abdomen appeared to be of about equal development. There were two foci in the left lung, one in the upper lobe the size of a small cherry, caseous with a fibrous border, another in the lower lobe slightly larger. The right upper lobe showed tuberculous broncho-pneumonia, the middle and lower many grey tubercles. The mediastinal glands on both sides were enlarged and caseous. The alimentary tract showed several tuberculous ulcers in the small intestine, and the corresponding mesenteric glands were in caseous adherent masses. There is apparently equal evidence for respiratory and alimentary portals, and the stage in each is about the same. Possibly the double route was taken nearly simultaneously.

No. 160. Male, aged 3 years.

Miliary tuberculosis of the lungs and meninges, a few also in the spleen. Two paratracheal glands were swollen and contained two small caseous foci, and one at the hilus was enlarged and caseous. No focus was found anywhere.

No. 164. Female, aged 6 years.

The difficulty in this case is to decide, in view of the widespread condition, which was the primary portal of entry. There were old-standing ulcers beneath each ear, with caseated and breaking-down cervical glands. The right lung showed several foci, certainly not of recent production, one the size of a pea, deep in the upper lobe, another similar at the base of the lowest; a small cavity in the middle, and, at the upper part of the lowest, a large focus the size of a cherry, caseous, with surrounding tubercles and early ulceration. In addition to these there were milia throughout the lungs. There were tuberculous ulcers in the intestines; the mesenteric glands were enlarged, caseous, adherent. The meninges showed numerous tubercles at the base and along the Sylvian fissures, more again below the cerebellum. The vertex and inter-hemispherical aspects showed tubercles in fair numbers. In spite of the lung condition the mediastinal glands, though containing tuberculous foci, were not nearly as much affected as the mesenteric. The respiratory and alimentary appeared to be of nearly equal age, as regards the foci; the miliary state of the lungs may be a secondary result of the intestinal. Doubtful whether: (i) Focal pulmonary, then intestinal, mesenteric, generalisation in lungs and thence the brain; or (ii) Primarily skin, then glands, blood-stream and generalisation; or (iii) Skin, lungs, intestines (the last two independently and simultaneously, as regards the focal state), and subsequent generalisation.

No. 178. Female, aged 10 years.

Miliary tuberculosis of both lungs, fairly numerous and evenly distributed, but rather more in the right lung. A gland at the right hilus and one paratracheal caseous. Nothing in the alimentary tract. A few miliary in the meninges, more at the base, but some also at the vertex. No focus detected anywhere.

No. 181. Female, aged 4 years.

Meninges showed general involvement, more aggregated at the base, in the interpeduncular space, along the Sylvian fissures, and below the cerebellum; few on the convexity. The lungs showed widespread miliary tubercles, more numerous in the right than the left. Mediastinal glands on the right were enlarged and caseous, but no focus was found.

No. 203. Male, aged 5 years.

Miliary tubercles scattered in moderate profusion and evenly through both lungs, but the source of these was not detected. The alimentary tract did not show any involvement, but one mesenteric gland was the size of a pea, and on section contained a minute caseous point. There was extensive tuberculous meningitis; at the base they were closely aggregated and pus was forming; there were also many along the Sylvian fissures and only a little less on the convexity. The ventricles contained more than the normal amount of fluid. No focus was found.

No. 206. Male, aged 16 months.

Grey tubercles in the upper lobe of each lung and less in the right middle lobe. The spleen showed a considerable number of miliary tubercles. The meninges were extensively affected; there was pus at the base with very numerous tubercles, also along the Sylvian fissures, in the velum interpositum and below the cerebellum. No focus was found, the other viscera yielding no evidence.

No. 210. Male, aged 5 years.

Here again no focus was found. The right lung contained miliary tubercles in the middle and lower lobes, and a gland at the hilus was caseated. The upper lobe of the left lung also contained miliary tubercles; there was no affection of the glands on the left; a few miliary were seen also in the spleen, while the meninges were extensively involved: tubercles were numerous at the base and along the Sylvian fissures, and there were one or two on the convexity and on the opposed surfaces of the cerebral hemispheres.

No. 211. Female, aged 5 years.

Apparently a haematogenous infection, but the primary focus was not found. The lesions were miliary tuberculosis of both lungs, the spleen, and the basal meninges.

No. 215. Female, aged 13 months.

The disease in this child was extensive and the decision as to the primary portal of entry a matter of opinion. There was a caseous focus as large as a filbert in the right lung, and grey tubercles throughout both lungs, while all groups of the mediastinal glands were enlarged and caseous. The cervical glands were a little affected. The mesenteric were in adherent caseous groups of about the same degree of involvement as the mediastinal; there were miliary tubercles of the liver and spleen, and a terminal meningitis. The mesentery and peritoneum generally were studded with tubercles. From the state of the glands in the thorax and abdomen there is no evidence for priority. The lung condition with a caseous focus of such a size must be of considerable standing, whereas the intestine itself showed one small ulcer only. On the other hand, the extensive affection of the peritoneum indicated that the abdominal condition was not very recent. On the whole, unless we regard the respiratory and alimentary as about coequal

in age, the most satisfactory explanation would be, the lung focus primarily, alimentary secondarily, thence the peritoneum and mesenteric glands, and via the thoracic duct to the pulmonary circulation and so setting up generalisation there, and via the blood-stream (systemic) to liver, spleen, and meninges.

No. 222. Female, aged 18 months.

Though the mediastinal glands on the right side were enlarged and caseous, no true focus was present in the lungs. The middle and lower lobes showed grey tubercles of the minute bronchioles, while the right upper and both lobes of the left contained miliary tubercles by the blood-stream. Some of the mesenteric glands were the size of a small pea and had caseous points. The liver, spleen, and kidney contained tubercles varying from small miliary to hempseed, and the base of the meninges showed them also. On the whole the sequence was probably : Respiratory first, causing the broncho-pneumonia of the lower lobes of the right lung, then alimentary to the mesenteric glands, without leaving signs in the intestine itself ; thence by the lymphatics to the pulmonary circulation and so miliary generalisation in the lungs, and from there to the liver, spleen, kidney, and meninges.

No. 223. Female, aged 4 years.

Extensive tuberculous meningitis, but no focus detected anywhere.

No. 227. Female, aged 3 years.

Lungs extensively affected with miliary and small grey tubercles, the right rather more than the left. There were numerous tubercles in the meninges, and a few in the liver and spleen, but no definite focus or indication of the primary portal of entry.

No. 230. Male, aged 3 years.

Tuberculous meningitis most severe, but the origin of this could not be traced. No focus was found, but there was miliary tuberculosis of the lungs, liver and spleen.

No. 239. Female, aged 3 years.

In this case the alimentary, as evidenced by the state of the mesenteric glands, would appear to be the oldest ; on the other hand the caseous focus in the left lung would be of older standing than the miliary and grey tubercles scattered generally throughout the lung. Also the mediastinal gland corresponding to the lung focus was completely caseous, like the mesenteric glands. The cerebellar focus was not very recent, less so than the miliary in the lungs and meninges. There are three possibilities : (i) Primary lung focus, alimentary secondarily, then generalisation in the lungs and from there to the meninges (if so, whence would the 'solitary' tubercle in the cerebellum arise, unless by separate earlier metastasis from the lung focus ?). (ii) Primary intestinal, secondary focus in lung and spread from there by inhalation to other parts of the lung, and by blood-stream to the cerebellum and meninges (but the cerebellar is a caseous node, while the meningeal affection is miliary and apparently recent). (iii) Lung and alimentary routes about the same time (judging from the glandular infection those in the thorax and those in the abdomen appear to be about the same stage), then from the lung to the cerebellum (focus), and from the mesenteric glands to the right side of the heart for the production of the miliary and grey tubercles in the lungs.

No. 275. Female, aged 6 years.

The lesions found were a general miliary infection of the right lung, and a few milia in the upper lobe of the left; an enlarged and caseated paratracheal gland on the right; sparse miliary tubercles in the spleen, and fairly thickly-studded miliary infection of the meninges, more aggregated at the base. No focus was discoverable, unless the mediastinal gland be regarded as such, but no evidence of the communication of this with a pulmonary vessel could be made out to account for the distribution in the lung, and there was certainly no focus in the lung to which this gland could be attributed.

No. 283. Male, aged 4 years.

The lungs in this case presented miliary tubercles, rather more in the right than the left, but not very numerous in either; the hilus on the right showed a large caseous gland, and one paratracheal on each side was caseated, that on the right being the larger. No focus was found in the lungs to account for these glands. There were a few miliary tubercles in the liver, more in the spleen. The meninges were severely affected, at the base and over the right hemisphere. In the latter, just below the cortex of the angular gyrus, was a mass of tubercles focally arranged, aggregating to the size of a large pea or small marble. The cerebral condition had probably arisen by vascular spread from the mediastinal gland, but the source of the latter was not found.

No. 291. Female, aged 4 years.

The only focus detected in this case was a caseous mass occupying nearly an entire pyramid at the lower part of the left kidney. There was miliary tuberculosis of the lungs, but no focus. No infection of the intestines; only one mesenteric gland showed anything and this was not so large as a haricot, but had a small caseous point. There were also a few milia in the liver. The kidney lesion was to all appearances the oldest, but whence this arose could not be discovered.

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